

WE CLAIM:

1. An anti-proliferative substance for preventing uncontrolled cellular proliferation, which comprises a radiolabeled DNA carrier, wherein a radioisotope is located internally within the DNA sequence, at 5' end or at 3' end, and wherein said radiolabeled DNA carrier penetrates cell membrane and is retained intracellularly for a time sufficient for the radioisotope to effect an efficient dose therapy.
2. The anti-proliferative substance according to Claim 1, wherein said carrier is an oligonucleotide.
3. The anti-proliferative substance according to Claim 2, wherein said oligonucleotide is linear.
4. The anti-proliferative substance according to Claim 1, wherein said carrier is a plasmid.
5. The anti-proliferative substance according to Claim 4, wherein said plasmid is circular.
6. The anti-proliferative substance according to Claim 5, wherein said plasmid is of viral or bacterial origin.
7. The anti-proliferative substance according to Claim 1, wherein said radioisotope is selected from the group consisting of ^{32}P , ^{33}P , ^{125}I , ^{131}I , ^{35}S , ^{198}Au , ^{90}Y , ^{89}Sr , ^{186}Re , ^{45}Ca and ^{153}Sm .
8. The anti-proliferative substance according to Claim 3, wherein said oligonucleotide is a double-

stranded DNA sequence or a single-stranded DNA sequence.

9. The anti-proliferative substance according to Claim 3, wherein said oligonucleotide is conjugated with an antibody for cell-specific delivery.

10. The anti-proliferative substance according to Claim 8, wherein said DNA oligonucleotide sequence is a single-stranded sense DNA sequence for hybridization to a specific genetic target.

11. The anti-proliferative substance according to Claim 8, wherein said DNA oligonucleotide sequence is a single-stranded antisense DNA sequence for hybridization to a specific genetic target.

12. The anti-proliferative substance according to Claim 1, which comprises DNA sequences of at least about 2 to about 2000 nucleotides.

13. The anti-proliferative substance according to Claim 12, wherein the DNA sequence is selected from the group consisting of

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CAC <u>GTT GAG GGG</u> CAT	(SEQ ID NO:1)
ATG <u>CCC CTC AAC</u> GTG	(SEQ ID NO:2)
GCC <u>CGA GAA CAT</u> CAT	(SEQ ID NO:3)
CCT <u>CGC AGT TTC</u> CAT	(SEQ ID NO:4)
AAA AAA AAA AAA AAA TTT	(SEQ ID NO:8)
TTT TTT TTT TTT TTT AAA	(SEQ ID NO:9)
CCC CCC CCC CCC CCC GGG	(SEQ ID NO:10)
CC GCG ACG ATG CCC CTC AAC GTT ACC ATC ACC	(SEQ ID NO:11)

wherein the radioisotope is located at any internal position in the sequence.

14. The anti-proliferative substance according to Claim 3, wherein the oligonucleotide is conjugated to at least one selected from the group consisting of a stent surface, cholesterol, oleic acid, linoleic acid, TGF α , antibody, TGF β , cytokines and growth factors.

15. The anti-proliferative substance according to Claim 13, wherein the radioisotope is selected from the group consisting of ^{32}P , ^{33}P , ^{125}I , ^{131}I , ^{35}S , ^{198}Au , ^{90}Y , ^{89}Sr , ^{186}Re , ^{45}Ca and ^{153}Sm .

16. A method for preparing a radiolabeled DNA carrier sequence wherein a radioisotope is located internally within the DNA sequence, which comprises the steps of:

- a) synthesizing a DNA sequence in at least two parts;
- b) labeling the 5' end of one of said two parts with a radioisotope;
- c) hybridizing said two parts of step b) with a sequence capable of hybridizing under stringent conditions; and
- d) ligating together said hybridized two parts.

17. The method of Claim 16, which further include a step e) after step d) to obtain a single-stranded radiolabeled DNA carrier, which comprises

- e) separating the hybridized DNA and recovering the radiolabeled DNA carrier sequence.

18. The method of Claim 12, which further include a step f) after step e) to obtain a double-stranded carrier having both strand radiolabeled, which comprises:

f) hybridizing together complementary radiolabeled single-stranded DNA carrier of step e).

19. The method of Claim 18, wherein said radioisotope is selected from the group consisting of ^{32}P , ^{33}P , ^{125}I , ^{131}I , ^{35}S , ^{198}AU , ^{90}Y , ^{89}SR , ^{186}Re , ^{45}Ca and ^{153}Sm .

20. The method of Claim 18, wherein said two parts of step a) form an antisense sequence and said sequence capable of hybridizing of step c) is a corresponding sense sequence.

21. The method of Claim 18, wherein said two parts of step a) form a sense sequence and said sequence capable of hybridizing of step c) is a corresponding antisense sequence.

22. Method for the prevention of uncontrolled cell proliferation in a mammal, which comprises delivering to said mammal a therapeutic substance according to Claim 1 *in situ* where said uncontrolled cell proliferation takes place.

23. Method according to Claim 22, wherein said uncontrolled cell proliferation is a restenosis following angioplasty, and said therapeutic substance is delivered by site-specific intravascular delivery.

24. Method according to Claim 23, wherein the therapeutic substance is coupled to an antibody.

25. Method according to Claim 22, wherein said uncontrolled cell proliferation is cancer or a

malignant tumor, and said therapeutic substance is coupled to a peptide moiety.

26. Method according to Claim 25, wherein said peptide moiety is selected from the group consisting of an antibody, TGF α , TGF β , cytokines and any growth factors.

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